

SEQUENCE LISTING

<110> Li, Chuan-Yuan
 Zhang, Xiuwu
 Dewhirst, Mark W
 5
 <120> A NOVEL siRNA-BASED APPROACH TO TARGET THE HIF-ALPHA FACTOR FOR
 GENE THERAPY
 10
 <130> 180-179 PCT
 <150> US 60/508,145
 <151> 2003-10-02
 15
 <160> 12
 <170> PatentIn version 3.3
 <210> 1
 20
 <211> 3958
 <212> DNA
 <213> Homo sapiens
 25
 <220>
 <221> CDS
 <222> (285)..(2765)
 <400> 1
 30
 gtgctgcctc gtctgagggg acaggaggat caccctcttc gtcgcttcgg ccagtgtgtc 60
 gggctggggc ctgacaagcc acctgaggag aggctcggag ccgggcccgg accccggcga 120
 ttgccgcccg cttctctcta gtctcacgag ggggtttccc cctcgacccc ccacctctgg 180
 35
 acttgccctt cttctctctt tccgcgtgtg gagggagcca gcgcttaggc cggagcgagc 240
 ctggggggccg cccgcccgtga agacatcgcg gggaccgatt cacc atg gag ggc gcc 296
 Met Glu Gly Ala
 40
 1
 ggc ggc gcg aac gac aag aaa aag ata agt tct gaa cgt cga aaa gaa 344
 Gly Gly Ala Asn Asp Lys Lys Lys Ile Ser Ser Glu Arg Arg Lys Glu
 5 10 15 20
 45
 aag tct cga gat gca gcc aga tct cgg cga agt aaa gaa tct gaa gtt 392
 Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys Glu Ser Glu Val
 25 30 35
 50
 ttt tat gag ctt gct cat cag ttg cca ctt cca cat aat gtg agt tcg 440
 Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His Asn Val Ser Ser
 40 45 50
 55
 cat ctt gat aag gcc tct gtg atg agg ctt acc atc agc tat ttg cgt 488
 His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile Ser Tyr Leu Arg
 55 60 65
 60
 gtg agg aaa ctt ctg gat gct ggt gat ttg gat att gaa gat gac atg 536
 Val Arg Lys Leu Leu Asp Ala Gly Asp Leu Asp Ile Glu Asp Asp Met
 70 75 80

	aaa gca cag atg aat tgc ttt tat ttg aaa gcc ttg gat ggt ttt gtt	584
	Lys Ala Gln Met Asn Cys Phe Tyr Leu Lys Ala Leu Asp Gly Phe Val	
	85 90 95 100	
5	atg gtt ctc aca gat gat ggt gac atg att tac att tct gat aat gtg	632
	Met Val Leu Thr Asp Asp Gly Asp Met Ile Tyr Ile Ser Asp Asn Val	
	105 110 115	
10	aac aaa tac atg gga tta act cag ttt gaa cta act gga cac agt gtg	680
	Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr Gly His Ser Val	
	120 125 130	
15	ttt gat ttt act cat cca tgt gac cat gag gaa atg aga gaa atg ctt	728
	Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met Arg Glu Met Leu	
	135 140 145	
20	aca cac aga aat ggc ctt gtg aaa aag ggt aaa gaa caa aac aca cag	776
	Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu Gln Asn Thr Gln	
	150 155 160	
25	cga agc ttt ttt ctc aga atg aag tgt acc cta act agc cga gga aga	824
	Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr Ser Arg Gly Arg	
	165 170 175 180	
30	act atg aac ata aag tct gca aca tgg aag gta ttg cac tgc aca ggc	872
	Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu His Cys Thr Gly	
	185 190 195	
35	cac att cac gta tat gat acc aac agt aac caa cct cag tgt ggg tat	920
	His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro Gln Cys Gly Tyr	
	200 205 210	
40	aag aaa cca cct atg acc tgc ttg gtg ctg att tgt gaa ccc att cct	968
	Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys Glu Pro Ile Pro	
	215 220 225	
45	cac cca tca aat att gaa att cct tta gat agc aag act ttc ctc agt	1016
	His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys Thr Phe Leu Ser	
	230 235 240	
50	cga cac agc ctg gat atg aaa ttt tct tat tgt gat gaa aga att acc	1064
	Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp Glu Arg Ile Thr	
	245 250 255 260	
55	gaa ttg atg gga tat gag cca gaa gaa ctt tta ggc cgc tca att tat	1112
	Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly Arg Ser Ile Tyr	
	265 270 275	
60	gaa tat tat cat gct ttg gac tct gat cat ctg acc aaa act cat cat	1160
	Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr Lys Thr His His	
	280 285 290	
65	gat atg ttt act aaa gga caa gtc acc aca gga cag tac agg atg ctt	1208
	Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln Tyr Arg Met Leu	
	295 300 305	
70	gcc aaa aga ggt gga tat gtc tgg gtt gaa act caa gca act gtc ata	1256
	Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln Ala Thr Val Ile	
	310 315 320	
75	-tat aac acc aag aat tct caa cca cag tgc att gta tgt gtg aat tac	1304
	Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val Cys Val Asn Tyr	
	325 330 335 340	

	gtt gtg agt ggt att att cag cac gac ttg att ttc tcc ctt caa caa	1352
	Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe Ser Leu Gln Gln	
	345 350 355	
5	aca gaa tgt gtc ctt aaa ccg gtt gaa tct tca gat atg aaa atg act	1400
	Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp Met Lys Met Thr	
	360 365 370	
10	cag cta ttc acc aaa gtt gaa tca gaa gat aca agt agc ctc ttt gac	1448
	Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser Ser Leu Phe Asp	
	375 380 385	
15	aaa ctt aag aag gaa cct gat gct tta act ttg ctg gcc cca gcc gct	1496
	Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu Ala Pro Ala Ala	
	390 395 400	
20	gga gac aca atc ata tct tta gat ttt ggc agc aac gac aca gaa act	1544
	Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn Asp Thr Glu Thr	
	405 410 415 420	
20	gat gac cag caa ctt gag gaa gta cca tta tat aat gat gta atg ctc	1592
	Asp Asp Gln Gln Leu Glu Glu Val Pro Leu Tyr Asn Asp Val Met Leu	
	425 430 435	
25	ccc tca ccc aac gaa aaa tta cag aat ata aat ttg gca atg tct cca	1640
	Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu Ala Met Ser Pro	
	440 445 450	
30	tta ccc acc gct gaa acg cca aag cca ctt cga agt agt gct gac cct	1688
	Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser Ser Ala Asp Pro	
	455 460 465	
35	gca ctc aat caa gaa gtt gca tta aaa tta gaa cca aat cca gag tca	1736
	Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro Asn Pro Glu Ser	
	470 475 480	
40	ctg gaa ctt tct ttt acc atg ccc cag att cag gat cag aca cct agt	1784
	Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp Gln Thr Pro Ser	
	485 490 495 500	
40	cct tcc gat gga agc act aga caa agt tca cct gag cct aat agt ccc	1832
	Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu Pro Asn Ser Pro	
	505 510 515	
45	agt gaa tat tgt ttt tat gtg gat agt gat atg gtc aat gaa ttc aag	1880
	Ser Glu Tyr Cys Phe Tyr Val Asp Ser Asp Met Val Asn Glu Phe Lys	
	520 525 530	
50	ttg gaa ttg gta gaa aaa ctt ttt gct gaa gac aca gaa gca aag aac	1928
	Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr Glu Ala Lys Asn	
	535 540 545	
55	cca ttt tct act cag gac aca gat tta gac ttg gag atg tta gct ccc	1976
	Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu Met Leu Ala Pro	
	550 555 560	
60	tat atc cca atg gat gat gac ttc cag tta cgt tcc ttc gat cag ttg	2024
	Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu Arg Ser Phe Asp Gln Leu	
	565 570 575 580	
60	tca cca tta gaa agc agt tcc gca agc cct gaa agc gca agt cct caa	2072
	Ser Pro Leu Glu Ser Ser Ser Ala Ser Pro Glu Ser Ala Ser Pro Gln	
	585 590 595	

	agc aca gtt aca gta ttc cag cag act caa ata caa gaa cct act gct Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln Glu Pro Thr Ala 600 605 610	2120
5	aat gcc acc act acc act gcc acc act gat gaa tta aaa aca gtg aca Asn Ala Thr Thr Thr Thr Ala Thr Thr Asp Glu Leu Lys Thr Val Thr 615 620 625	2168
10	aaa gac cgt atg gaa gac att aaa ata ttg att gca tct cca tct cct Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala Ser Pro Ser Pro 630 635 640	2216
15	acc cac ata cat aaa gaa act act agt gcc aca tca tca cca tat aga Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser Ser Pro Tyr Arg 645 650 655 660	2264
20	gat act caa agt cgg aca gcc tca cca aac aga gca gga aaa gga gtc Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala Gly Lys Gly Val 665 670 675	2312
	ata gaa cag aca gaa aaa tct cat cca aga agc cct aac gtg tta tct Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro Asn Val Leu Ser 680 685 690	2360
25	gtc gct ttg agt caa aga act aca gtt cct gag gaa gaa cta aat cca Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu Glu Leu Asn Pro 695 700 705	2408
30	aag ata cta gct ttg cag aat gct cag aga aag cga aaa atg gaa cat Lys Ile Leu Ala Leu Gln Asn Ala Gln Arg Lys Arg Lys Met Glu His 710 715 720	2456
35	gat ggt tca ctt ttt caa gca gta gga att gga aca tta tta cag cag Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr Leu Leu Gln Gln 725 730 735 740	2504
40	cca gac gat cat gca gct act aca tca ctt tct tgg aaa cgt gta aaa Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp Lys Arg Val Lys 745 750 755	2552
	gga tgc aaa tct agt gaa cag aat gga atg gag caa aag aca att att Gly Cys Lys Ser Ser Glu Gln Asn Gly Met Glu Gln Lys Thr Ile Ile 760 765 770	2600
45	tta ata ccc tct gat tta gca tgt aga ctg ctg ggg caa tca atg gat Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly Gln Ser Met Asp 775 780 785	2648
50	gaa agt gga tta cca cag ctg acc agt tat gat tgt gaa gtt aat gct Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys Glu Val Asn Ala 790 795 800	2696
55	cct ata caa ggc agc aga aac cta ctg cag ggt gaa gaa tta ctc aga Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu Glu Leu Leu Arg 805 810 815 820	2744
	gct ttg gat caa gtt aac tga gctttttctt aatttcattc ctttttttg Ala Leu Asp Gln Val Asn 825	2795
60	acactggtgg ctcaactacct aaagcagttct atttatattt tctacatcta attttagaag	2855
	cctggctaca atactgcaca aacttgggtta gttcaatttt tgateccctt tctacttaat	2915

ttacattaat gctctttttt agtatgttct ttaatgctgg atcacagaca gctcattttc 2975
 tcagtttttt ggtatttaaa ccattgcatt gcagtagcat catttttaaaa aatgcacctt 3035
 5 tttatttatt tatttttggc tagggagttt atcccttttt cgaattattt ttaagaagat 3095
 gccaatataa tttttgtaag aaggcagtaa cctttcatca tgatcatagg cagttgaaaa 3155
 10 atttttacac cttttttttt acattttaca taaataataa tgctttgccca gcagtacgtg 3215
 gtagccacaa ttgcacaata tattttctta aaaaatacca gcagttactc atggaatata 3275
 ttctgctgtt ataaaactag tttttaagaa gaaatttttt ttggcctatg aaattgttaa 3335
 15 acctggaaca tgacattgtt aatcatataa taatgattct taaatgctgt atggttttatt 3395
 atttaaatgg gtaaagccat ttacataata tagaaagata tgcatatatc tagaaggat 3455
 gtggcattta tttggataaa attctcaatt cagagaaatc atctgatgtt tctatagtca 3515
 20 ctttgccagc tcaaaagaaa acaataccct atgtagtgtt ggaagtttat gctaatttg 3575
 tgtaactgat attaaaccta aatgttctgc ctaccctgtt ggtataaaga tattttgagc 3635
 25 agactgtaaa caagaaaaaa aaaatcatgc attccttagca aaattgccta gtatgttaat 3695
 ttgctcaaaa tacaatgttt gattttatgc actttgtcgc tattaacatc ctttttttca 3755
 tgtagatttc aataattgag taattttaga agcattattt taggaatata tagttgtcac 3815
 30 agtaaatac ttgttttttc tatgtacatt gtacaaattt ttcattcctt ttgctctttg 3875
 tggttggatc taacactaac tgtattgttt tgttacatca aataaacatc ttctgtggac 3935
 35 caggaaaaaa aaaaaaaaaa aaa 3958

<210> 2
 <211> 826
 40 <212> PRT
 <213> Homo sapiens
 <400> 2

45 Met Glu Gly Ala Gly Gly Ala Asn Asp Lys Lys Lys Ile Ser Ser Glu
 1 5 10 15

50 Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys
 20 25 30

55 Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His
 35 40 45

60 Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile
 50 55 60

65 Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Asp Leu Asp Ile
 65 70 75 80

Glu Asp Asp Met Lys Ala Gln Met Asn Cys Phe Tyr Leu Lys Ala Leu
 85 90 95

5 Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly Asp Met Ile Tyr Ile
 100 105 110

10 Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr
 115 120 125

15 Gly His Ser Val Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met
 130 135 140

Arg Glu Met Leu Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu
 145 150 155 160

20 Gln Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr
 165 170 175

25 Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu
 180 185 190

30 His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro
 195 200 205

35 Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys
 210 215 220

Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys
 225 230 235 240

40 Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp
 245 250 255

45 Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly
 260 265 270

50 Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr
 275 280 285

55 Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln
 290 295 300

Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln
 305 310 315 320

60 Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val
 325 330 335

Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe
 340 345 350

5 Ser Leu Gln Gln Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp
 355 360 365

10 Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser
 370 375 380

15 Ser Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu
 385 390 395 400

Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn
 405 410 415

20 Asp Thr Glu Thr Asp Asp Gln Gln Leu Glu Glu Val Pro Leu Tyr Asn
 420 425 430

25 Asp Val Met Leu Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu
 435 440 445

30 Ala Met Ser Pro Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser
 450 455 460

35 Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro
 465 470 475 480

Asn Pro Glu Ser Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp
 485 490 495

40 Gln Thr Pro Ser Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu
 500 505 510

45 Pro Asn Ser Pro Ser Glu Tyr Cys Phe Tyr Val Asp Ser Asp Met Val
 515 520 525

50 Asn Glu Phe Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr
 530 535 540

55 Glu Ala Lys Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu
 545 550 555 560

Met Leu Ala Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu Arg Ser
 565 570 575

60 Phe Asp Gln Leu Ser Pro Leu Glu Ser Ser Ser Ala Ser Pro Glu Ser
 580 585 590

Ala Ser Pro Gln Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln
 595 600 605
 5 Glu Pro Thr Ala Asn Ala Thr Thr Thr Thr Ala Thr Thr Asp Glu Leu
 610 615 620
 10 Lys Thr Val Thr Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala
 625 630 635 640
 15 Ser Pro Ser Pro Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser
 645 650 655
 Ser Pro Tyr Arg Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala
 660 665 670
 20 Gly Lys Gly Val Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro
 675 680 685
 25 Asn Val Leu Ser Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu
 690 695 700
 30 Glu Leu Asn Pro Lys Ile Leu Ala Leu Gln Asn Ala Gln Arg Lys Arg
 705 710 715 720
 35 Lys Met Glu His Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr
 725 730 735
 Leu Leu Gln Gln Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp
 740 745 750
 40 Lys Arg Val Lys Gly Cys Lys Ser Ser Glu Gln Asn Gly Met Glu Gln
 755 760 765
 45 Lys Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly
 770 775 780
 50 Gln Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys
 785 790 795 800
 55 Glu Val Asn Ala Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu
 805 810 815
 Glu Leu Leu Arg Ala Leu Asp Gln Val Asn
 820 825
 60
 <210> 3
 <211> 3973
 <212> DNA
 <213> Mus musculus


```

<220>
<221> CDS
5 <222> (258) .. (2768)

<400> 3
cgcgaggagact gtccctcgccg ccgtcgcgagg cagtgtcttag ccaggccttg acaagctagc      60
10 cggaggagcg cctaggaacc cgagccggag ctcagcgagc gcagcctgca cgcccgcctc      120
    gcgtcccggg ggggtcccg cccccacccc gcctctggac ttgtctcttt ccccgcgcg      180
    gcggacagag ccggcgttta ggcccagcg agcccggggg ccgccggccg ggaagacaac      240
15 gcggggcaccg attcgcc atg gag ggc gcc ggc ggc gag aac gag aag aaa      290
    Met Glu Gly Ala Gly Gly Glu Asn Glu Lys Lys
    1 5 10
20 aag atg agt tct gaa cgt cga aaa gaa aag tct aga gat gca gca aga      338
    Lys Met Ser Ser Glu Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg
    15 20 25
25 tct cgg cga agc aaa gag tct gaa gtt ttt tat gag ctt gct cat cag      386
    Ser Arg Arg Ser Lys Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln
    30 35 40
    ttg cca ctt ccc cac aat gtg agc tca cat ctt gat aaa gct tct gtt      434
    Leu Pro Leu Pro His Asn Val Ser Ser His Leu Asp Lys Ala Ser Val
    45 50 55
30 atg agg ctc acc atc agt tat tta cgt gtg aga aaa ctt ctg gat gcc      482
    Met Arg Leu Thr Ile Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala
    60 65 70 75
35 ggt ggt cta gac agt gaa gat gag atg aag gca cag atg gac tgt ttt      530
    Gly Gly Leu Asp Ser Glu Asp Glu Met Lys Ala Gln Met Asp Cys Phe
    80 85 90
40 tat ctg aaa gcc cta gat ggc ttt gtg atg gtg cta aca gat gac ggc      578
    Tyr Leu Lys Ala Leu Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly
    95 100 105
45 gac atg gtt tac att tct gat aac gtg aac aaa tac atg ggg tta act      626
    Asp Met Val Tyr Ile Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr
    110 115 120
    cag ttt gaa cta act gga cac agt gtg ttt gat ttt act cat cca tgt      674
    Gln Phe Glu Leu Thr Gly His Ser Val Phe Asp Phe Thr His Pro Cys
    125 130 135
50 gac cat gag gaa atg aga gaa atg ctt aca cac aga aat ggc cca gtg      722
    Asp His Glu Glu Met Arg Glu Met Leu Thr His Arg Asn Gly Pro Val
    140 145 150 155
55 aga aaa ggg aaa gaa cta aac aca cag cgg agc ttt ttt ctc aga atg      770
    Arg Lys Gly Lys Glu Leu Asn Thr Gln Arg Ser Phe Phe Leu Arg Met
    160 165 170
60 aag tgc acc cta aca agc cgg ggg agg acg atg aac atc aag tca gca      818
    Lys Cys Thr Leu Thr Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala
    175 180 185

```

	acg tgg aag gtg ctt cac tgc acg ggc cat att cat gtc tat gat acc	866
	Thr Trp Lys Val Leu His Cys Thr Gly His Ile His Val Tyr Asp Thr	
	190 195 200	
5	aac agt aac caa cct cag tgt ggg tac aag aaa cca ccc atg acg tgc	914
	Asn Ser Asn Gln Pro Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys	
	205 210 215	
10	ttg gtg ctg att tgt gaa ccc att cct cat ccg tca aat att gaa att	962
	Leu Val Leu Ile Cys Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile	
	220 225 230 235	
15	cct tta gat agc aag aca ttt ctc agt cga cac agc ctc gat atg aaa	1010
	Pro Leu Asp Ser Lys Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys	
	240 245 250	
20	ttt tct tac tgt gat gaa aga att act gag ttg atg ggt tat gag ccg	1058
	Phe Ser Tyr Cys Asp Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro	
	255 260 265	
25	gaa gaa ctt ttg ggc cgc tca att tat gaa tat tat cat gct ttg gat	1106
	Glu Glu Leu Leu Gly Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp	
	270 275 280	
30	tct gat cat ctg acc aaa act cac cat gat atg ttt act aaa gga caa	1154
	Ser Asp His Leu Thr Lys Thr His His Asp Met Phe Thr Lys Gly Gln	
	285 290 295	
35	gtc acc aca gga cag tac agg atg ctt gcc aaa aga ggt gga tat gtc	1202
	Val Thr Thr Gly Gln Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val	
	300 305 310 315	
40	tgg gtt gaa act caa gca act gtc ata tat aat acg aag aac tcc cag	1250
	Trp Val Glu Thr Gln Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln	
	320 325 330	
45	cca cag tgc att gtg tgt gtg aat tat gtt gta agt ggt att att cag	1298
	Pro Gln Cys Ile Val Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln	
	335 340 345	
50	cac gac ttg att ttc tcc ctt caa caa aca gaa tct gtg ctc aaa cca	1346
	His Asp Leu Ile Phe Ser Leu Gln Gln Thr Glu Ser Val Leu Lys Pro	
	350 355 360	
55	gtt gaa tct tca gat atg aag atg act cag ctg ttc acc aaa gtt gaa	1394
	Val Glu Ser Ser Asp Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu	
	365 370 375	
60	tca gag gat aca agc tgc ctt ttt gat aag ctt aag aag gag cct gat	1442
	Ser Glu Asp Thr Ser Cys Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp	
	380 385 390 395	
65	gct ctc act ctg ctg gct cca gct gcc ggc gac acc atc atc tct ctg	1490
	Ala Leu Thr Leu Leu Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu	
	400 405 410	
70	gat ttt ggc agc gat gac aca gaa act gaa gat caa caa ctt gaa gat	1538
	Asp Phe Gly Ser Asp Asp Thr Glu Thr Glu Asp Gln Gln Leu Glu Asp	
	415 420 425	
75	gtt cca tta tat aat gat gta atg ttt ccc tct tct aat gaa aaa tta	1586
	Val Pro Leu Tyr Asn Asp Val Met Phe Pro Ser Ser Asn Glu Lys Leu	
	430 435 440	

	aat ata aac ctg gca atg tct cct tta cct tca tcg gaa act cca aag	1634
	Asn Ile Asn Leu Ala Met Ser Pro Leu Pro Ser Ser Glu Thr Pro Lys	
	445 450 455	
5	cca ctt cga agt agt gct gat cct gca ctg aat caa gag gtt gca tta	1682
	Pro Leu Arg Ser Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu	
	460 465 470 475	
10	aaa tta gaa tca agt cca gag tca ctg gga ctt tct ttt acc atg ccc	1730
	Lys Leu Glu Ser Ser Pro Glu Ser Leu Gly Leu Ser Phe Thr Met Pro	
	480 485 490	
15	cag att caa gat cag cca gca agt cct tct gat gga agc act aga caa	1778
	Gln Ile Gln Asp Gln Pro Ala Ser Pro Ser Asp Gly Ser Thr Arg Gln	
	495 500 505	
20	agt tca cct gag aga ctt ctt cag gaa aac gta aac act cct aac ttt	1826
	Ser Ser Pro Glu Arg Leu Leu Gln Glu Asn Val Asn Thr Pro Asn Phe	
	510 515 520	
25	tcc cag cct aac agt ccc agt gaa tat tgc ttt gat gtg gat agc gat	1874
	Ser Gln Pro Asn Ser Pro Ser Glu Tyr Cys Phe Asp Val Asp Ser Asp	
	525 530 535	
25	atg gtc aat gta ttc aag ttg gaa ctg gtg gaa aaa ctg ttt gct gaa	1922
	Met Val Asn Val Phe Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu	
	540 545 550 555	
30	gac aca gag gca aag aat cca ttt tca act cag gac act gat tta gat	1970
	Asp Thr Glu Ala Lys Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp	
	560 565 570	
35	ttg gag atg ctg gct ccc tat atc cca atg gat gat gat ttc cag tta	2018
	Leu Glu Met Leu Ala Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu	
	575 580 585	
40	cgt tcc ttt gat cag ttg tca cca tta gag agc aat tct cca agc cct	2066
	Arg Ser Phe Asp Gln Leu Ser Pro Leu Glu Ser Asn Ser Pro Ser Pro	
	590 595 600	
45	cca agt atg agc aca gtt act ggg ttc cag cag acc cag tta cag aaa	2114
	Pro Ser Met Ser Thr Val Thr Gly Phe Gln Gln Thr Gln Leu Gln Lys	
	605 610 615	
45	cct acc atc act gcc act gcc acc aca act gcc acc act gat gaa tca	2162
	Pro Thr Ile Thr Ala Thr Ala Thr Thr Thr Ala Thr Thr Asp Glu Ser	
	620 625 630 635	
50	aaa aca gag acg aag gac aat aaa gaa gat att aaa ata ctg att gca	2210
	Lys Thr Glu Thr Lys Asp Asn Lys Glu Asp Ile Lys Ile Leu Ile Ala	
	640 645 650	
55	tct cca tct tct acc caa gta cct caa gaa acg acc act gct aag gca	2258
	Ser Pro Ser Ser Thr Gln Val Pro Gln Glu Thr Thr Thr Ala Lys Ala	
	655 660 665	
60	tca gca tac agt ggc act cac agt cgg aca gcc tca cca gac aga gca	2306
	Ser Ala Tyr Ser Gly Thr His Ser Arg Thr Ala Ser Pro Asp Arg Ala	
	670 675 680	
	gga aag aga gtc ata gaa cag aca gac aaa gct cat cca agg agc ctt	2354
	Gly Lys Arg Val Ile Glu Gln Thr Asp Lys Ala His Pro Arg Ser Leu	
	685 690 695	

5	aag ctg tct gcc act ttg aat caa aga aat act gtt cct gag gaa gaa	2402
	Lys Leu Ser Ala Thr Leu Asn Gln Arg Asn Thr Val Pro Glu Glu Glu	
	700 705 710 715	
10	tta aac cca aag aca ata gct tgc cag aat gct cag agg aag cga aaa	2450
	Leu Asn Pro Lys Thr Ile Ala Ser Gln Asn Ala Gln Arg Lys Arg Lys	
	720 725 730	
15	atg gaa cat gat ggc tcc ctt ttt caa gca gca gga att gga aca tta	2498
	Met Glu His Asp Gly Ser Leu Phe Gln Ala Ala Gly Ile Gly Thr Leu	
	735 740 745	
20	ttg cag caa cca ggt gac tgt gca cct act atg tca ctt tcc tgg aaa	2546
	Leu Gln Gln Pro Gly Asp Cys Ala Pro Thr Met Ser Leu Ser Trp Lys	
	750 755 760	
25	cga gtg aaa gga ttc ata tct agt gaa cag aat gga acg gag caa aag	2594
	Arg Val Lys Gly Phe Ile Ser Ser Glu Gln Asn Gly Thr Glu Gln Lys	
	765 770 775	
30	act att att tta ata ccc tcc gat tta gca tgc aga ctg ctg ggg cag	2642
	Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly Gln	
	780 785 790 795	
35	tca atg gat gag agt gga tta cca cag ctg acc agt tac gat tgt gaa	2690
	Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys Glu	
	800 805 810	
40	gtt aat gct ccc ata caa ggc agc aga aac cta ctg cag ggt gaa gaa	2738
	Val Asn Ala Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu Glu	
	815 820 825	
45	tta ctc aga gct ttg gat caa gtt aac tga gcgtttccta atctcattcc	2788
	Leu Leu Arg Ala Leu Asp Gln Val Asn	
	830 835	
50	ttttgattgt taatgttttt gttcagttgt tgttgtttgt tgggtttttg tttctgttgg	2848
	ttattttttgg aactggtgg ctcagcagtc tatttatatt ttctatatct aatttttagaa	2908
	gcctggctac aatactgcac aaactcagat agtttagttt tcatcccctt tctacttaat	2968
55	tttcattaat gctcttttta atatgttctt ttaatgccag atcacagcac attcacagct	3028
	cctcagcatt tcaccattgc attgctgtag tgtcatttaa aatgcacctt tttatttatt	3088
	tattttttggg gagggagttt gtcccttatt gaattatttt taatgaaatg ccaatataat	3148
60	tttttaagaa agcagtaaat tctcatcatg atcataggca gttgaaaact ttttactcat	3208
	ttttttcatg ttttacctga aaataatgct ttgtcagcag tacatggtag ccacaattgc	3268
65	acaatatatt ttcttttaaaa aaccagcagc tactcatgca atatattctg catttataaa	3328
	actagttttt aagaaatttt ttttggccta tggaattggt aagcctggat catgaagcgt	3388
	tgatcttata atgattctta aactgtatgg tttctttata tgggtaaagc cattttacatg	3448
70	atataaagaa atatgcttat atctggaagg tatgtggcat ttatttggat aaaattctca	3508
	attcagagaa gttatctggg gtttcttgac tttaccaact caaaacagtc cctctgtagt	3568
	tgtggaagct tatgctaata ttgtgtaatt gattatgaaa cataaatgtt ctgcccaccc	3628

5 tggttggtata aagacatddd gagcatactg taaacaaaca aacaaaaaat catgctttgt 3688
 tagtaaaatt gcctagtatg ttgatttggt gaaaatatga tgtttggttt tatgcacttt 3748
 gtcgctatta acatcctttt ttcatataga tttcaataag tgagtaattt tagaagcatt 3808
 atdtttaggaa tatagagttg tcatagtaaa catcttggtt tttctatgta cactgtataa 3868
 10 atdtttcggt cccttgctct ttgtgggttg gtctaact aactgtactg ttttggtata 3928
 tcaaataaac atcttctgtg gaccaggaaa aaaaaaaaaa aaaaa 3973

15 <210> 4
 <211> 836
 <212> PRT
 <213> Mus musculus

20 <400> 4

Met Glu Gly Ala Gly Gly Glu Asn Glu Lys Lys Lys Met Ser Ser Glu
 1 5 10 15

25 Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys
 20 25 30

30 Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His
 35 40 45

35 Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile
 50 55 60

40 Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Gly Leu Asp Ser
 65 70 75 80

45 Glu Asp Glu Met Lys Ala Gln Met Asp Cys Phe Tyr Leu Lys Ala Leu
 85 90 95

50 Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly Asp Met Val Tyr Ile
 100 105 110

55 Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr
 115 120 125

60 Gly His Ser Val Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met
 130 135 140

Arg Glu Met Leu Thr His Arg Asn Gly Pro Val Arg Lys Gly Lys Glu
 145 150 155 160

Leu Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr
 165 170 175

Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu
 180 185 190
 5
 His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro
 195 200 205
 10
 Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys
 210 215 220
 15
 Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys
 225 230 235 240
 20
 Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp
 245 250 255
 Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly
 260 265 270
 25
 Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr
 275 280 285
 30
 Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln
 290 295 300
 35
 Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln
 305 310 315 320
 40
 Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val
 325 330 335
 Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe
 340 345 350
 45
 Ser Leu Gln Gln Thr Glu Ser Val Leu Lys Pro Val Glu Ser Ser Asp
 355 360 365
 50
 Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser
 370 375 380
 55
 Cys Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu
 385 390 395 400
 60
 Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asp
 405 410 415
 Asp Thr Glu Thr Glu Asp Gln Gln Leu Glu Asp Val Pro Leu Tyr Asn
 420 425 430

Asp Val Met Phe Pro Ser Ser Asn Glu Lys Leu Asn Ile Asn Leu Ala
 435 440 445
 5 Met Ser Pro Leu Pro Ser Ser Glu Thr Pro Lys Pro Leu Arg Ser Ser
 450 455 460
 10 Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Ser Ser
 465 470 475 480
 15 Pro Glu Ser Leu Gly Leu Ser Phe Thr Met Pro Gln Ile Gln Asp Gln
 485 490 495
 20 Pro Ala Ser Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu Arg
 500 505 510
 Leu Leu Gln Glu Asn Val Asn Thr Pro Asn Phe Ser Gln Pro Asn Ser
 515 520 525
 25 Pro Ser Glu Tyr Cys Phe Asp Val Asp Ser Asp Met Val Asn Val Phe
 530 535 540
 30 Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr Glu Ala Lys
 545 550 555 560
 35 Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu Met Leu Ala
 565 570 575
 40 Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu Arg Ser Phe Asp Gln
 580 585 590
 Leu Ser Pro Leu Glu Ser Asn Ser Pro Ser Pro Pro Ser Met Ser Thr
 595 600 605
 45 Val Thr Gly Phe Gln Gln Thr Gln Leu Gln Lys Pro Thr Ile Thr Ala
 610 615 620
 50 Thr Ala Thr Thr Thr Ala Thr Thr Asp Glu Ser Lys Thr Glu Thr Lys
 625 630 635 640
 55 Asp Asn Lys Glu Asp Ile Lys Ile Leu Ile Ala Ser Pro Ser Ser Thr
 645 650 655
 60 Gln Val Pro Gln Glu Thr Thr Thr Ala Lys Ala Ser Ala Tyr Ser Gly
 660 665 670
 Thr His Ser Arg Thr Ala Ser Pro Asp Arg Ala Gly Lys Arg Val Ile
 675 680 685

Glu Gln Thr Asp Lys Ala His Pro Arg Ser Leu Lys Leu Ser Ala Thr
 690 695 700

5
 Leu Asn Gln Arg Asn Thr Val Pro Glu Glu Glu Leu Asn Pro Lys Thr
 705 710 715 720

10
 Ile Ala Ser Gln Asn Ala Gln Arg Lys Arg Lys Met Glu His Asp Gly
 725 730 735

15
 Ser Leu Phe Gln Ala Ala Gly Ile Gly Thr Leu Leu Gln Gln Pro Gly
 740 745 750

20
 Asp Cys Ala Pro Thr Met Ser Leu Ser Trp Lys Arg Val Lys Gly Phe
 755 760 765

Ile Ser Ser Glu Gln Asn Gly Thr Glu Gln Lys Thr Ile Ile Leu Ile
 770 775 780

25
 Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly Gln Ser Met Asp Glu Ser
 785 790 795 800

30
 Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys Glu Val Asn Ala Pro Ile
 805 810 815

35
 Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu Glu Leu Leu Arg Ala Leu
 820 825 830

40
 Asp Gln Val Asn
 835

45
 <210> 5
 <211> 55
 <212> DNA
 <213> Artificial

50
 <220>
 <221> misc_feature
 <222> (20)..(28)
 <223> n can be any nucleotide, up to 4 of which can be missing,
 55 representing a single stranded loop of from 5-9 bases, the
 hairpin loop remaining single-stranded when bases 1-19 and 29-47
 hybridize to each other to form a duplex

60
 <220>
 <221> misc_feature
 <222> (48)..(55)
 <223> n can be any nucleotide, up to 6 of which can be missing,
 representing a 3' overhang of from 2-8 nucleotides, the 3'
 overhang remaining single stranded when the duplex forms between

nucleotides 1-19 and 29-47

5 <400> 5
gatgacatga aagcacagan nnnnnnnntc tgtgctttca tgtcatcnnn nnnnn 55

10 <210> 6
 <211> 53
 <212> DNA
 <213> Artificial

15 <220>
 <223> Specific sequence of an siRNA used to target human HIF-1a

20 <220>
 <221> misc_feature
 <222> (1)..(19)
 <223> Sense strand of an siRNA used to target human HIF-1a. Sequence
corresponds to bases 528-546 of Genbank Accession No. NM_001530.
This sequence forms the double stranded region of a hairpin by
intramolecular hybridization with bases 29-47.

25 <220>
 <221> misc_feature
 <222> (20)..(28)
 <223> 9 base loop structure, whichs stays single stranded when bases
1-19 and 29-47 form a duplex

30 <220>
 <221> misc_feature
 <222> (29)..(47)
 <223> Antisense strand of an siRNA used to target human HIF-1a.
Sequence corresponds to the reverse complement of bases 528-546
35 of NM_001530. This sequence forms the double stranded region of
a hairpin by intramolecular hybridization with bases 1-19.

40 <220>
 <221> misc_feature
 <222> (48)..(53)
 <223> 6 base 3' overhang, which stays single stranded when bases 1-19
and 29-47 form a duplex

45 <400> 6
gatgacatga aagcacagat tcaagagatc tgtgctttca tgtcatcttt ttt 53

50 <210> 7
 <211> 19
 <212> DNA
 <213> Homo sapiens

55 <400> 7
atgacatgaa agcacagat 19

60 <210> 8
 <211> 21
 <212> DNA
 <213> Artificial

 <220>
 <223> Artificial sense strand designed with no known homology to any
human gene to be used to create a negative control siRNA

	<400> 8		21
	aattctccga acgtgtcacg t		
5			
	<210> 9		
	<211> 21		
	<212> DNA		
10	<213> Homo sapiens		
	<400> 9		21
	tcaagatcat tgctcctcct g		
15			
	<210> 10		
	<211> 21		
	<212> DNA		
	<213> Homo sapiens		
20			
	<400> 10		21
	ctgcttgctg atccacatct g		
25			
	<210> 11		
	<211> 21		
	<212> DNA		
	<213> Homo sapiens		
30			
	<400> 11		21
	ctgatcatct gacaaaaact c		
35			
	<210> 12		
	<211> 22		
	<212> DNA		
	<213> Homo sapiens		
40			
	<400> 12		22
	gtttcaaccc agacatatcc ac		